Proposed Decision Memo for Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085R7)

Decision Summary

The Centers for Medicare and Medicaid Services (CMS) proposes the following:

Based on the Food and Drug Administration (FDA) clearance of new embolic protection devices, we propose to revise the NCD language regarding embolic protection devices as follows:

Coverage is limited to procedures performed using FDA approved carotid artery stents and FDA approved or cleared embolic protection devices.

The use of an FDA approved or cleared embolic protection device is required. If deployment of the embolic protection device is not technically possible, then the procedure should be aborted given the risks of CAS without embolic protection.

We propose to make no changes in coverage of patient groups for percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting (Medicare National Coverage Determination (NCD) Manual 20.7B4). We propose to retain our existing coverage for the following with a slight revision to the language regarding embolic protection devices:

- Patients who are at high risk for carotid endarterectomy (CEA) and who also have symptomatic carotid artery stenosis ≥70%. Coverage is limited to procedures performed using FDA-approved carotid artery stenting systems and FDA-approved or cleared embolic protection devices;
- Patients who are at high risk for CEA and have symptomatic carotid artery stenosis between 50% and 70%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on carotid artery stenting (CAS) post-approval studies (Medicare NCD Manual 20.7B);
- Patients who are at high risk for CEA and have asymptomatic carotid artery stenosis ≥80%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on CAS post- approval studies (Medicare NCD Manual 20.7B).

We are requesting public comments on this proposed determination pursuant to Section 1862(l) of the Social Security Act. After considering the public comments, we will make a final determination and issue a final decision memorandum.

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Proposed Decision Memo

TO: Administrative File CAG-00085R7

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SUBJECT: Proposed Coverage Decision Memorandum for Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085R7)

DATE: September 10, 2009

I. Proposed Decision

The Centers for Medicare and Medicaid Services (CMS) proposes the following:

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We propose to make no changes in coverage of patient groups for percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting (Medicare National Coverage Determination (NCD) Manual 20.7B4). We propose to retain our existing coverage for the following with a slight revision to the language regarding embolic protection devices:

- Patients who are at high risk for carotid endarterectomy (CEA) and who also have symptomatic carotid artery stenosis ≥70%. Coverage is limited to procedures performed using FDA-approved carotid artery stenting systems and FDA-approved or cleared embolic protection devices;
- Patients who are at high risk for CEA and have symptomatic carotid artery stenosis between 50% and 70%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on carotid artery stenting (CAS) post-approval studies (Medicare NCD Manual 20.7B);
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We are requesting public comments on this proposed determination pursuant to Section 1862(l) of the Social Security Act. After considering the public comments, we will make a final determination and issue a final decision memorandum.

II. Background

CMS internally generated a reconsideration request for PTA of the carotid artery concurrent with stenting. In the last reconsideration on this topic on October 14, 2008 (CAG-000856) CMS stated that "[w]e are aware of other data that has yet to be published and strongly urge that publication at the soonest possible time. We will work with any requestor as soon as that data is published to determine the need for an expedited review and reconsideration." New data has recently been published that examines outcomes in patients for whom coverage is currently limited to participation in clinical trials and post approval studies. In this reconsideration, CMS will examine whether coverage should be expanded to beneficiaries who are at high risk for CEA due to anatomic risk factors with asymptomatic carotid artery stenosis of ≥ 80% when CAS procedures are performed outside of clinical trials, FDA approved IDE trials or FDA approved post approval studies.

Under the current policy patients at high risk for carotid endarterectomy (CEA) who have symptomatic carotid artery stenosis ≥ 70% are covered for procedures performed using FDA approved CAS systems with embolic protection devices in facilities approved by CMS to perform CAS procedures. In addition, patients at high risk for CEA with symptomatic carotid artery stenosis between 50% and 70% and patients at high risk for CEA with asymptomatic carotid artery stenosis ≥ 80% are covered in accordance with the Category B Investigational Device Exemption (IDE) clinical trials regulation (42, CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on CAS post approval studies (Medicare NCD Manual 20.7, B3).

III. History of Medicare Coverage

Over the past eight years, Medicare has expanded coverage for PTA and stenting of the carotid artery. Medicare first covered PTA of the carotid artery concurrent with stent placement in accordance with the Food and Drug Administration (FDA) approved protocols governing Category B Investigational Device Exemption (IDE) clinical trials and later in FDA required post approval studies (Medicare NCD Manual 20.7B2, B3).

Effective March 17, 2005, Medicare expanded coverage for PTA and stenting of the carotid artery when performed on patients at high risk for CEA who also have symptomatic carotid artery stenosis ≥ 70% only when performed in a CMS approved facility for CAS with FDA-approved carotid artery stenting systems and embolic protection devices. Symptoms of carotid artery stenosis include carotid transient ischemic attack (TIA) (distal focal neurological dysfunction persisting less than 24 hours), non-disabling stroke (Modified Rankin Scale score < 3 with symptoms for 24 hours or more), and transient monocular blindness (amaurosis fugax) (Medicare NCD Manual 20.7B4).

Effective April 30, 2007, Medicare maintained the existing coverage policy and included detailed facility recertification instructions in the NCD.

Effective October 14, 2008, Medicare maintained the existing coverage policy, making no deletions, revisions or additions.

Medicare's NCD for PTA concurrent with carotid stenting can be found in NCD Manual 20.7. Medicare's NCD for PTA concurrent with carotid stenting in FDA approved post approval studies can also be found in NCD Manual 20.7B3.

Benefit Category Determination

For an item or service to be covered by the Medicare program, it must meet one of the statutorily defined benefit categories outlined in the Social Security Act. PTA of the carotid artery concurrent with stenting, at a minimum, falls under the benefit categories set forth in section §1861(b) (inpatient hospital services), a part A benefit under §1812(a)(1) and §1861(s)(1) (physician services), a part B benefit. This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.

IV. Timeline of Recent Activities

March 18, 2009	CMS internally generated a reconsideration request to examine newly published evidence.
April 17, 2009	Initial 30-day public comment period closed.
September 10, 2009	Proposed decision memorandum posted; 30-day comment period begins.

V. FDA Status

There are currently seven carotid stent systems with Premarket Approval (PMA) from the FDA plus five distal filter embolic protection devices (EPDs) and one distal balloon occlusion EPD with FDA 510(k) clearance. Recent FDA 510(k) cleared EPDs include one proximally placed flow reversal EPD and one distally placed filter with focal suction.[1,2]

VI. General Methodological Principles

When making national coverage decisions, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

A detailed account of the methodological principles of study design that the agency utilizes to assess the relevant literature on a therapeutic or diagnostic item or service for specific conditions can be found in Appendix A. In general, features of clinical studies that improve quality and decrease bias include the selection of a clinically relevant cohort, the consistent use of a single good reference standard, and the blinding of readers of the index test, and reference test results.

Public comments sometimes cite the published clinical evidence and give CMS useful information. Public comments that give information on unpublished evidence such as the results of individual practitioners or patients are less rigorous and therefore less useful for making a coverage determination. Public comments that contain personal health information will not be made available to the public. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

VII. Evidence

A. Introduction

In this coverage analysis, we considered carotid artery stenting studies and evidence that were published since the last reconsideration in 2008. It incorporates all evidence from prior decision memoranda regarding this issue. A summary of the body of evidence reviewed to date in developing this proposed decision memorandum is available via the final decision memoranda released following the completion of each of the prior national coverage analyses (NCAs) for reconsiderations of the CAS NCD. For carotid artery stenting, we believe that studies should evaluate health outcomes especially in patients who do not have symptoms from carotid artery disease. Health outcomes for carotid artery stenting include death, stroke, myocardial infarction and other adverse events.

As noted in the two prior reconsiderations of this topic, we have considered the professional society guidance that the accepted standards for carotid revascularization should apply to CAS if it is to be considered an alternative to CEA. Professional guidelines developed and published by the American Heart Association (AHA) (Sacco, et al., 2006; Goldstein et al., 2006) identify these benchmarks and suggest that CEA is indicated in patients with asymptomatic and symptomatic carotid artery stenosis when surgeons can achieve perioperative morbidity and mortality rates that are < 3% and < 6% respectively. Similar periprocedural rates would be expected to demonstrate that CAS improves health outcomes.

Literature Search

Because this is a reconsideration, CMS focused on new clinical research studies, technology assessments, guidelines and reviews published since the October 14, 2008 decision memorandum, but also considered literature addressing the patient populations under consideration which was published prior to the 2008 NCD. CMS searched PubMed from January 2008 to June 2009. General keywords included carotid artery stenting, carotid artery angioplasty, risk factors (high risk for surgery and anatomic risk factors). Abstracts without a complete publication were excluded. Using these general parameters, 9 original studies, 2 systematic reviews and 3 sets of evidence based guidelines were found.

B. Discussion of evidence reviewed

1. Evidence Questions

Our determination of whether to expand coverage of carotid artery stenting for high risk asymptomatic patients under Medicare involves consideration of health outcomes. For this NCD, the questions of interest are:

a. Is the evidence sufficient to conclude that percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting for asymptomatic patients at high risk for CEA with carotid artery stenosis ≥ 80% improves health outcomes compared to carotid endarterectomy or optimal medical therapy outside the clinical trial or post market study setting?

b. Is the evidence sufficient to conclude that percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting for asymptomatic patients with anatomic high risk factors with carotid artery stenosis ≥ 80% and symptomatic patients with carotid artery stenosis 50-70% improves health outcomes?

2. External Technology Assessments

Ederle J, Featherstone RL, Brown MB. Randomized controlled trials comparing endarterectomy and endovascular treatment for carotid artery stenosis: a Cochrane systematic review. Stroke 2009;40:1373-1380.

Ederle and colleagues reported the results of a Cochrane systematic review "to assess the benefits and risks of endovascular treatment compared to surgery." This review provided an update of the Cochrane review done by the same authors in 2007 which reported that the data were "limited and conflicting" and concluded that: "The data support the continuing inclusion of patients within randomized clinical trials between endovascular and surgical treatment for carotid artery stenosis. Randomisation should continue in the ongoing trials and centres not participating in the large multicentre trials should be encouraged to randomise suitable patients locally. This could contribute to any future meta-analysis."

For the current review, randomized trials on stenting compared to endarterectomy were selected. Ten trials (n=3178 patients) were included in the analysis. The primary outcome was stroke or death within 30 days. Intention to treat analysis was used.The Peto fixed effect model was used to calculate odds ratios. The authors found: "Using a fixed-effect model, the odds ratio (OR) for the combined outcome of death or any stroke was significantly in favor of carotid endarterectomy (OR endovascular:surgery 1.40, 95% CI 1.04 to 1.88, P = 0.03)." Identical to the 2007 review, they concluded: The data are difficult to interpret because the trials are heterogeneous. Five trials were stopped early, perhaps leading to an overestimate of the risks of endovascular treatment. The results do not support a change in clinical practice away from recommending carotid endarterectomy as the treatment of choice for suitable carotid artery stenosis but support continued recruitment in the large ongoing trials." Only randomized trials were included so the published registry studies were not.

3. Internal Technology Assessment

Chiam PTL, Roubin GS, Panagopoulos G, Iyer SS, Green RM, Brennan C, Vitek JJ. One-year clinical outcomes, midterm survival, and predictors of mortality after carotid stenting in elderly patients. Circulation 2009;119:2343 -2348.

Chiam and colleagues reported the results of a case series (n=142) of elderly patients who underwent CAS from 2003 to 2007 "to determine survival and predictors of mortality of selected elderly patients after stenting." Inclusion criteria were age ≥ 80 years and symptomatic ≥ 50% diameter stenosis or asymptomatic stenosis ≥ 70%. Patients were non high risk patients. The outcomes included combined death and stroke at 30 days and death at 12 months. Mean age was 83 years. Men comprised 61%. Symptomatic patients comprised 28%.

The authors reported: "Among the 153 procedures, 5 events (1 death, 2 major strokes, 2 minor strokes) occurred, resulting in an overall 30-day stroke or death rate of 3.3% (5.1% in the symptomatic group, 2.6% in asymptomatic patients)." At 12 months, 15 (12%) deaths occurred out of 129 patients with at least 1 year of follow-up. The authors concluded: "This study demonstrates that in selected elderly patients, a high proportion (85%) survived 2 years and >75% survived 3 years after stenting. Carotid stenting may be considered a revascularization option in such patients. Better selection of patients using the predictors of mortality may help to reduce unwarranted procedures and to optimize survival likelihood." Limitations of case series such as selection issues and lack of controls are applicable. Results by symptomatology and anatomic risk factors were not reported. At 12 months, there were 15 deaths and 1 nonfatal stroke for a combined 12.4% (16/129) rate. Although these patients were considered non high risk, the authors noted: "Elderly patients undergoing CS, however, may not represent the "average" elderly patient. No data on survival after CS in elderly patients are available."

de Donato G, Setacci C, Deloose K, Peeters P, Cremonesi A, Bosiers M. Long-term results of carotid artery stenting. J Vasc Surg 2008;48:1431-1441.

de Donato and colleagues reported the results of an analysis of a registry of 4 European carotid high volume centers (n=3179) "to review long-term results after carotid stent implantation in a large cohort of patients." Patients were non high risk who underwent CAS from 1998 to 2006. Inclusion criteria included "symptomatic lesions ≥ 50%, asymptomatic lesions ≥ 80%, calculated according to the North American Symptomatic Carotid Endarterectomy Trial [NASCET] criteria." Outcomes included death, stroke or other neurological complications. Mean age was about 72 years. Men comprised 67%. Symptomatic patients comprised 41%.

The authors reported: "At 5 years freedom from mortality, stroke-related death, ipsilateral fatal/major stroke, and any stroke rate were 82%, 93.5%, 93.3%, and 91.9%, respectively." Rates of all cause mortality and any stroke increased year to year and were similar for symptomatic and asymptomatic patients. The authors concluded: "Our long-term results in a large cohort of patients validated CAS as a durable procedure for stroke prevention. The annual rate of neurological complications after CAS was comparable to that of conventional surgery as demonstrated by large RCTs involving both symptomatic patients (North American Symptomatic Carotid Endarterectomy Trial [NASCET] and European Carotid Surgery Trial [ECST]) and asymptomatic patients (Asymptomatic Carotid Atherosclerosis Study [ACAS] and Asymptomatic Carotid Surgery Trial [ACST])." Limitations of registry studies such as voluntary reporting, selection and lack of controls are applicable. The stroke and death proportions for asymptomatic patients were 3.5%, 8.2%, 15.4%, 20.1% and 26.1% from years 1 to 5 respectively. The authors reported a 1.9% annual rate of stroke. Results by anatomic risk factors were not reported.

Ederle J, Featherstone RL, Brown MM, CAVATAS collaborators. Long-term outcome of endovascular treatment versus medical care for carotid artery stenosis in patients not suitable for surgery and randomized in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS). Cerebrovascular Diseases 2009;23:1-7.

Ederle and colleagues reported the results of a randomized controlled trial of patients (n=40) considered unsuitable for carotid endarterectomy in CAVATAS to compare endovascular treatment of carotid stenosis to medical treatment. Patients included in CAVATAS had the "presence of clinically important carotid stenosis" as determined by the individual site investigators. Patients considered unsuitable for CAVATAS had "recent myocardial infarction, poorly controlled, hypertension or diabetes mellitus, renal disease, respiratory failure, inaccessible carotid stenosis, or severe cervical spondylosis" and were randomized (1:1) to carotid intervention (n=20) or medical therapy (n=20) for this subset trial (CAVATAS-MED). Of the 40 patients, 17 patients had surgical contraindications, 14 had medical contraindications, 7 refused surgery and 2 had unrecorded reasons for why they were considered unsuitable for surgery. Primary outcome was death and stroke in the follow-up period. Patients were enrolled from 1992 to 1997. Intention to treat analysis was used. Mean age was about 69 years. Men comprised 78%. Symptomatic patients comprised 63%. Median follow-up was 4.5 years.

The authors found 1 death or stroke within 30 days in the endovascular treatment group and 0 death or stroke within 30 days in the medical group. At any time during the follow-up period, there were 9 death or stroke events in both groups. The authors concluded: "We failed to show superiority of endovascular treatment above medical care alone for carotid stenosis in a very small group of patients not suitable for surgical treatment. However, the trial randomized only 40 patients, and was therefore severely underpowered to detect clinically relevant treatment differences. Ongoing trials of carotid stenting will need to demonstrate improved safety and efficacy before endovascular treatment should enter routine practice." In this report, the inclusion criteria were not well defined. Since enrollment started before stents were available, endovascular treatment was variable. The actual number of patients who underwent CAS was not reported. Medical therapy also was not uniformly defined. Results for symptomatic and asymptomatic patients were not reported separately.

Gray WA, Chaturvedi S, Verta P, on behalf of the Investigators and the Executive Committees. Thirty-day outcomes for carotid artery stenting in 6320 patients from 2 prospective, multicenter, high-surgical-risk registries. Circ Cardiovasc Intervent 2009;2:159-166.

Gray and colleagues reported the results of a combined analysis of "2145 patients from the Emboshield and Xact Post Approval Carotid Stent Trial (EX) and 4175 patients from the Carotid ACCULINK/ACCUNET Post Approval Trial to Uncover Rare Events (C2)." The objective was to evaluate how outcomes from CAS compared to perioperative morbidity (stroke) and mortality recommendations from the American Heart Association and the American Stroke Association on prevention of stroke in symptomatic and asymptomatic patients (see guidelines in section 5 below). Patients were high-surgical risk individuals who underwent CAS from 2004 to 2006 and had symptomatic (≥ 50% stenosis) or asymptomatic (≥ 80% stenosis) lesions. Of the 6370 patients enrolled in the EX[3] and C2[4] postmarket surveillance studies mandated by the FDA, 6320 patients were included in the analytical dataset. The EX study involved 253 investigators at 128 sites while the C2 study involved 519 investigators at 186 sites. The primary end point of both studies was a composite of death, stroke or myocardial infarction within 30 days of CAS. Mean age was about 73 years. Men comprised about 62% of the studies. Patient with symptoms of carotid artery stenosis comprised about 12%.

The authors reported: "The 30-day primary composite end point (hierarchical) of death, stroke, and MI for EX was 4.1% (95% CI, 3.3% to 5.1%), for C2 was 3.7% (95% CI, 3.1% to 4.3%), and for the combined studies was 3.8% (95% CI, 3.4% to 4.3%). The 30-day combined end point of death and stroke rate for EX was 4.1% (95% CI, 3.3% to 5.0%), 3.4% (95% CI, 2.9% to 4.0%) for C2, and 3.6% (95% CI, 3.2% to 4.1%) for the combined population. For the combined symptomatic population the rate of 30-day death and stroke was 6.4% (95% CI, 4.8% to 8.4%), and for the combined asymptomatic population it was 3.2% (95% CI, 2.8% to 3.7%)."

A subgroup analysis of patients with anatomic high surgical risk factors ("history of CEA, radiation, therapy to the neck or radical neck surgery, surgically inaccessible lesion at or above the C2 vertebra or below the clavicle, lesions obstructed by tumors in the neck, spinal immobility/inability to flex neck beyond neutral or kyphotic deformity, the presence of a tracheostomy stoma, and contralateral laryngeal nerve palsy") was also performed. They reported: "The 30-day rate of death and stroke for the 60 symptomatic patients with anatomic factors was 1.7% (95% CI, 0.0% to 8.9%); the single stroke was adjudicated as major. The 30-day rate of death and stroke for the 371 asymptomatic patients with anatomic high-risk features was 2.7% (95% CI, 1.3% to 4.9%), of which 78% were minor."

The authors concluded: "Outcomes for carotid artery stenting in nonoctogenarian high-surgical-risk patients have improved since the pivotal Food and Drug Administration approval trials, and have achieved American Heart Association standards in both symptomatic and asymptomatic lesions." They also reported: "This study also carries the limitations of any registry analysis, including limited follow-up duration and the potential for bias in end point detection. Given that any prophylactic procedure requires the patient to survive long enough to reap the benefit of reduced end point events to justify procedural or surgical risk (as per the AHA guidelines document stipulation of an expected 5-year survival), no definitive statements regarding the ultimate benefit of CAS can be made absent long-term follow-up in this population. Last, the separation of patients between high-risk anatomic and physiological features is complex because of the need to rank order the risk factors for categorization (ie, a patient may have both an anatomic and physiological risk), resulting in almost twice the number of octogenarians in the physiological group, and potentially contributing to an increase in outcome events in this cohort."

Kawabata Y, Sakai N, Nagata I, Horikawa F, Miyake H, Ueno Y, Kikuchi H. Clinical predictors of transient ischemic attack, stroke, or death within 30 days of carotid artery stent placement with distal balloon protection. J Vasc Interv Radiol 2009;20:9–16.

Kawabata and colleagues reported the results of a case series of 58 patients who underwent carotid artery stenting from 1999 to 2008 "to determine potential clinical risk factors for the development of postprocedural neurologic deficits after carotid artery stent placement." Inclusion criteria included ≥ 50% carotid stenosis if they had recurrent stroke or ≥ 60% carotid asymptomatic stenosis with bilateral carotid lesions or multiple-vessel disease. Primary outcome was combined 30 day major adverse events. Of the 58 patients, 41 were high risk while 17 were low risk. Mean age was 70 years. Men comprised 84%. Symptomatic patients comprised 52%.

The authors reported: "Six patients (9.0%) experienced a TIA and one patient (1.5%) had a major stroke (1.5%) within 30 days of the procedure." The 30 day stroke and death rate was 1.5%. They concluded: "Our data suggest that carotid artery stent placement with distal balloon protection can be performed with similar periprocedural complication rates as CEA. CEA should be the first-line treatment in the management of patients older than 75 years of age." Limitations inherent to case studies are applicable. Sample size was small. Low risk patients were included which may lead to reduced 30 day events. Anatomic high risk factors were not evaluated.

Massop D, Dave R, Metzger C, Bachinsky W, Solis M, Shah M, et al. Stenting and angioplasty with protection in patients at high-risk for endarterectomy: SAPPHIRE Worldwide Registry first 2,001 patients. Catheterization and Cardiovascular Interventions 2009;73:129–136.

Massop and colleagues reported the results of an interim analysis of the SAPPHIRE[5](Stenting and Angioplasty with Protection of Patients with High Risk for Endarterectomy) Worldwide registry (n=2001) "to evaluate 30-day outcomes after CAS utilizing the CASES training program within a broader number of centers and an increased number of physicians performing the procedure." The SAPPHIRE Worldwide registry (SAPPHIRE WW[6]) is a post market study being conducted at 350 clinical sites (216 contributed data) in the U.S. and Canada. The primary end point was a composite of death, stroke or myocardial infarction within 30 days of CAS. High surgical risk patients were required to have "either ≥ 50% carotid stenosis (as determined by ultrasound or angiogram) if symptomatic (TIA or stroke within 180 days of the procedure) or ≥ 80% carotid stenosis (as determined by ultrasound or angiogram) if asymptomatic." Of the 2001 patients enrolled from 2006 to 2008, 1620 had complete 30 day follow up data and were included in the analysis. Mean age was about 72 years. Men comprised 62%. Patients with symptoms of carotid stenosis comprised 28%.

The authors reported: "The cumulative incidence of MAE at 30 days was 4.4% (95% CI 3.5%, 5.3%), a rate comparable to the MAE rates in previous studies." The rate of death and stroke was 4.0% at 30 days. They also reported: "Asymptomatic patients with anatomic risk factors had a 30-day stroke and death rate of 1.8% while symptomatic patients with anatomic risk factors had a 30-day rate of 4.5% (P=0.0589)." They concluded: "While the number of physicians performing CAS continues to increase, MAE rates seen in this registry (4.4%) are well within an acceptable range, as was first seen in the SAPPHIRE randomized trial (4.8%). A significant decrease in MAE was seen in patients with anatomic risk compared with physiologic risk factors. The SAPPHIRE Worldwide Registry supports the use of CAS as an alternative to CEA in patients who are at high-risk for surgery due to anatomic risk factors." Overall results were not reported separately for asymptomatic and symptomatic patients. The most common anatomic risk factors were previous CEA restenosis and contralateral carotid occlusion. Limitations of registry studies such as voluntary reporting, selection and lack of controls are applicable.

Sidawy AN,Zwolak RM, White RA, Siami FS, Schermerhorn ML, Sicard GA, et al. Risk-adjusted 30-day outcomes of carotid stenting and endarterectomy: Results from the SVS Vascular Registry. J Vasc Surg 2009;49:71-79.

Sidawy and colleagues reported the results of an analysis of the Society for Vascular Surgery (SVS) Vascular Registry (VR), the "the first operational societal registry of carotid procedures" with 1450 CAS patients, "to report the feasibility of the VR and to provide the baseline demographics and risk-adjusted 30-day outcomes of CAS and CEA." Patients were high-surgical-risk patients who have symptomatic (≥50% stenosis) or asymptomatic (≥80% stenosis) lesions who underwent carotid intervention from 2005 to 2007. The VR contained data from 287 providers at 56 centers at time of the publication. The primary outcome was combined death, stroke and myocardial infarction at 30 days. Of the CAS patients, mean age was about 71 years.Men comprised 60%. Symptomatic patients comprised 44%.

The authors reported: "For CAS, death/stroke/MI at 30 days was 7.13% for symptomatic patients and 4.60% for asymptomatic patients (P=.04)." The combined rate was 5.7% (83/1450) and the death and stroke rate at 30 days was 5.6% (81/1450). The authors concluded: "Following best possible risk adjustment of these unmatched groups, symptomatic and asymptomatic CAS patients had significantly higher 30-day postprocedure incidence of death/stroke/MI when compared with CEA patients. The initial 1.5 years of data collection provide proof of concept that a specialty society based VR can succeed in meeting regulatory and scientific goals. With continued enrollment and follow-up, analysis of SVS-VR will supplement randomized trials by providing real-world comparisons of CAS and CEA with sufficient numbers to serve as an outcome assessment tool of important patient subsets and across the spectrum of peripheral vascular procedures." Results by anatomic risk factors were not reported. Limitations of registry studies such as voluntary reporting, selection and lack of controls are applicable.

Simonetti G, Gandini R, Versaci F, Pampana E, Fabiano S, Stefanini M, et al. Carotid artery stenting: findings based on 8 years' experience. Radiol med 2009;114:95–110.

Simonetti and colleagues reported the results of a registry of 1003 patients who underwent CAS from 1999 to 2007 to evaluate 30 day death and stroke. Inclusion criteria were symptomatic stenosis > 50% and asymptomatic lesions with stenosis > 70%, in agreement with the NASCET criteria. Primary outcome was combined 30 day death and stroke. Mean age was 70 years. Men comprised 58%. High risk patients "refused by surgeons" comprised 24%. Symptomatic patients comprised 52%.

The authors reported: "The 30-day transient ischaemic attack (TIA)/stroke/death rate was 2.16%: death (0.18%) major stroke (0.45%) and minor stroke/TIA (1.53%). During a follow-up up to 8 years, restenoses occurred in 39 cases (3.57%), of which 28 were post-CAS (2.57%) and 11 post-CAS performed for restenosis after carotid endarterectomy (1%)." Limitations of registry studies such as voluntary reporting, selection and lack of controls are applicable. Low risk patients were included which may lead to reduced adverse event rates. Definitions of low and high risk were not specified. Anatomic high risk factors were not evaluated.

Steppacher R, Csikesz N, Eslami M, Arous E, Messina L, Schanzer A. An analysis of carotid artery stenting procedures performed in New York and Florida (2005-2006): Procedure indication, stroke rate, and mortality rate are equivalent for vascular surgeons and nonvascular surgeons. J Vasc Surg 2009;49:1379-86.

Steppacher and colleagues reported the results of an analysis of inpatient data from New York and Florida (n=4001) to compare "the indications, in-patient mortality rate, and in-patient stroke rate for patients undergoing CAS, according to operator specialty." Patients were identified by querying inpatient databases from the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Health Care Research and Quality (AHRQ) for International Classification of Disease (ICD)-9-CM codes 00.63 (carotid artery stenting) and 00.61 (carotid artery angioplasty) from 2005-2006. Outcomes included inpatient death and stroke. Symptomatic patients were identified using codes for "transient ischemic attack, amaurosis fugax, or stroke at the time of admission." Mean age was about 71 years. Men comprised 62%. Symptomatic patients comprised 9%.

The authors reported overall inhospital mortality and stoke of 2.0%. For symptomatic patients (n=348), the inhospital mortality and stroke was 7.8%. The authors concluded: "Despite a paucity of level 1 evidence for CAS in asymptomatic patients and current Centers for Medicare and Medicaid Services (CMS) policy limiting reimbursement for CAS to only high-risk symptomatic patients, VS (vascular surgeons) and non-VS are treating primarily asymptomatic patients. Perioperative rates of stroke and death are equivalent between VS, IC (interventional cardiologists), and IR (interventional radiologists). Regional variation of operator type is substantial, and despite similar outcomes, < 50% of CAS is performed by VS." Results for asymptomatic patients were not reported.Limitations include those inherent to hospital discharge databases, coding accuracy, difficulties classifying symptom class and lack of data on degree of stenosis. Data were only available for the hospital stays which may not reflect 30 day outcomes in many instances.

Usman AA, Tang GL, Eskandari MK. Metaanalysis of procedural stroke and death among octogenarians: carotid stenting versus carotid endarterectomy. J Am Coll Surg 2009;208:1124-1131.

Usman and colleagues conducted "a metaanalysis on 41 sets of data from peer-reviewed published articles on CAS versus CEA in octogenarians from 1997 to 2007" and "compared the primary outcomes measures of periprocedural (30-day) myocardial infarction (MI), stroke, and death after CAS or CEA in patients aged 80 years or greater for all studies." Studies were included if 10 or more procedures were performed, 30 day outcomes were reported and 30 day complication rates were available. Eight stenting studies (826 patients) and 33 endarterectomy studies (7017 patients) were evaluated. The authors reported: "In conclusion, octogenarians undergoing CAS had a 3.46-times higher absolute risk of stroke than those undergoing CEA, with no significant difference in mortality and a trend toward a lower rate of MI. Further outcomes research and risk stratification analyses are needed to help guide clinical decision-making. But given that the purpose of carotid intervention is stroke prevention, CAS in octogenarians using current technology should be avoided in favor of CEA or possibly medical management unless a stroke rate of less than 3% can be achieved."

Vogel TR, Dombrovskiy VY, Haser PB, Haser PB, Scheirer JC, Graham AM. Outcomes of carotid artery stenting and endarterectomy in the United States. J Vasc Surg 2009;49:325-330.

Vogel and colleagues reported the results of an analysis of carotid artery stenting outcomes based on inpatient data from the 2005 Nationwide Inpatient Sample (NIS) "to evaluate national outcomes of CAS and CEA and to compare utilization and outcomes of these procedures in different age groups." The NIS is an "all-payer hospital database developed as part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Health Care Research and Quality (AHRQ)." Patients were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure code 00.63 for CAS. The analytic database included 6569 patients aged 60 years and older who underwent CAS. Mean age was about 73 years. Men comprised 62%. Symptomatic patients comprised 2.9% (189/6569) and were identified using codes for transient cerebral ischemia, transient paralysis of limb, transient arterial occlusion, transient visual loss, amaurosis fugax and other generalized ischemic cerebrovascular disease.

The authors reported: "The overall incidence of stroke was 4.16% after CAS and 2.66% after CEA (P < .0001). CAS was more often utilized in octogenarians than in younger patients (8.55% in 80+ vs 7.92% in 60-69 years; P < .0002). Increased age was not associated with greater stroke rates after CAS or CEA (P=.19 and .06, respectively). Octogenarians, compared to younger patients, had greater cardiac, pulmonary, and renal complications after CEA (3.0% vs 1.9%, 1.9% vs 1.0%, and 1.4% vs 0.54%, respectively; P < .0001)." They found a death and stroke rate of 298/6569 (4.5%) during the inpatient stay for CAS and concluded: "Octogenarians did not have a higher risk of stroke after CAS when compared to younger patients. Stroke was the strongest predictor of hospital mortality. The increased utilization of CAS in the aged, which had significantly higher stroke rates in all age groups studied, may account for the greater hospital mortality seen after CAS in the elderly. Further studies focused on the aged are needed to define the best management strategies in the elderly." Results were not reported by symptomatology although there were very few patients identified as symptomatic patients. Limitations include those inherent to hospital discharge databases, coding accuracy, difficulties classifying symptom class and lack of data on degree of stenosis. Data were only available for the hospital stays which may not reflect 30 day outcomes in many instances.

4. MedCAC

No Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) was convened for this issue.

5.Evidence-based guidelines

Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD, Culebras A, DeGraba TJ, Gorelick PB, Guyton JR, Hart RG, Howard G, Kelly-Hayes M, Nixon JVI, Sacco RL. Primary prevention of ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council: Cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Stroke 2006;37:1583-1633.

This guideline provided "an overview of the evidence on various established and potential stroke risk factors and provides recommendations for the reduction of stroke risk." Specifically for asymptomatic carotid stenosis, the authors stated:

"It is recommended that patients with asymptomatic carotid artery stenosis be screened for other treatable causes of stroke and that intensive therapy of all identified stroke risk factors be pursued (Class I, Level of Evidence C). The use of aspirin is recommended unless contraindicated because aspirin was used in all of the cited trials as an antiplatelet drug except in the surgical arm of 1 study, in which there was a higher rate of MI in those who were not given aspirin (Class I, Level of Evidence B). Prophylactic carotid endarterectomy is recommended in highly selected patients with high-grade asymptomatic carotid stenosis performed by surgeons with < 3% morbidity/mortality rates (Class I, Level of Evidence A). Patient selection should be guided by an assessment of comorbid conditions and life expectancy, as well as other individual factors, and be balanced by an understanding of the overall impact of the procedure if all-cause mortality is considered as one of the end points, and it should include a thorough discussion of the risks and benefits of the procedure with an understanding of patient preferences. Carotid angioplasty–stenting might be a reasonable alternative to endarterectomy in asymptomatic patients at high risk for the surgical procedure (Class IIb, Level of Evidence B); however, given the reported periprocedural and overall 1-year event rates, it remains uncertain whether this group of patients should have either procedure."

Liapis CD, Bell PRF, Mikhailidis D, Sivenius J, Nicolaides A, Fernandes J, Biasi G, Norgren L, on behalf of the ESVS Guidelines Collaborators. ESVS guidelines. Invasive treatment for carotid stenosis: indications, techniques. Eur J Vasc Endovasc Surg 2009;37:S1-S19.

Liapis and colleagues reported the European Society for Vascular Surgery evidence based guidelines on carotid stenosis interventions. They used the Agency for Healthcare Research and Quality (AHRQ) grading recommendations[7] and reported: "The European Society for Vascular Surgery brought together a group of experts in the field of carotid artery disease to produce updated guidelines for the invasive treatment of carotid disease. The recommendations were rated according to the level of evidence. Carotid endarterectomy (CEA) is recommended in symptomatic patients with > 50% stenosis if the perioperative stroke/death rate is < 6% [A], preferably within 2 weeks of the patient's last symptoms [A]. CEA is also recommended in asymptomatic men < 75 years old with 70-99% stenosis if the perioperative stroke/death risk is < 3% [A]. The benefit from CEA in asymptomatic women is significantly less than in men [A]. CEA should therefore be considered only in younger, fit women [A]. Carotid patch angioplasty is preferable to primary closure [A]. Aspirin at a dose of 75-325 mg daily and statins should be given before, during and following CEA. [A] Carotid artery stenting (CAS) should be performed only in high-risk for CEA patients, in high-volume centres with documented low peri-operative stroke and death rates or inside a randomized controlled trial [C]. CAS should be performed under dual antiplatelet treatment with aspirin and clopidogrel [A]. Carotid protection devices are probably of benefit [C]."

Sacco RL, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, et al. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: A statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: Co-Sponsored by the Council on Cardiovascular Radiology and Intervention: The American Academy of Neurology affirms the value of this guideline. Stroke 2006:37;577-617.

This guideline provided "recommendations on the prevention of ischemic stroke among survivors of ischemic stroke or transient ischemic attack." Specific recommendations were as follows:

1. "For patients with recent TIA or ischemic stroke within the last 6 months and ipsilateral severe (70% to 99%) carotid artery stenosis, CEA by a surgeon with a perioperative morbidity and mortality of < 6% (Class I, Level of Evidence A) is recommended. For patients with recent TIA or ischemic stroke and ipsilateral moderate (50% to 69%) carotid stenosis, CEA is recommended, depending on patient-specific factors such as age, gender, comorbidities, and severity of initial symptoms (Class I, Level of Evidence A). When the degree of stenosis is < 50%, there is no indication for CEA (Class III, Level of Evidence A) (Table 4)."

2. "When CEA is indicated for patients with TIA or stroke, surgery within 2 weeks is suggested rather than delaying surgery (Class IIa, Level of Evidence B)."

3. "Among patients with symptomatic severe stenosis (> 70%) in whom the stenosis is difficult to access surgically, medical conditions are present that greatly increase the risk for surgery, or other specific circumstances exist such as radiation-induced stenosis or restenosis after CEA, CAS is not inferior to endarterectomy and may be considered (Class IIb, Level of Evidence B). CAS is reasonable when performed by operators with established periprocedural morbidity and mortality rates of 4% to 6%, similar to that observed in trials of CEA and CAS (Class IIa, Level of Evidence B)."

4. "Among patients with symptomatic carotid occlusion, EC/IC bypass surgery is not routinely recommended (Class III, Level of Evidence A)."

6.Professional Society Position Statements

No new professional society position statements have been released since the last reconsideration of this policy.

7. Public Comments

During the initial 30-day comment period CMS received 79 comments. Comments in support of a coverage expansion were in the majority, but they present a diverse array of suggestions for coverage of various patient populations falling both within FDA approved indications and outside of those indications. The comments received from CAS stakeholders are summarized first followed by the remaining public comments with and without evidence. A complete list of references cited by commenters is available in the appendices.

Stakeholder Comments

American Academy of Neurology (AAN), Neurovascular Coalition (NVC), Society of Vascular and Interventional Neurology (SVIN), Society of NeuroInterventional Surgery (SNIS), Society of Interventional Radiology (SIR)

The public comments submitted by these professional societies were nearly identical with only slight variations in each. They each reference Gray et al., 2009, and all societies except the SVIN reference McPhee et al., 2008 and Sidawy et al,, 2009 in support of their recommendations for expanded coverage. The societies note that data from Gray et al., 2009 is concerning for patients at high risk due to "physiological factors" (actually the presence of comorbid disease) who had a 3.2% stroke and death rate in 30 days. They also note that the stroke and death rate is likely higher as patients in EXACT with restenosis were included in the physiologic high risk group rather than the anatomic high risk group. Regarding the McPhee and Sidawy results, they state that the data "are concerning for the significantly worse outcomes from CAS versus CEA and data, suggesting that for CAS outcomes outside of the trial setting may be less likely to meet AHA benchmarks."

Based on data from these studies, the societies agree that coverage should be expanded for asymptomatic patients who are < 80 years old with > 80% stenosis with anatomic high risk factors only if facilities are required to participate in a multispecialty accrediting program that requires facility outcomes to meet AHA benchmarks. They note that currently such an accrediting program does not yet exist but is currently under development and is supported by numerous specialty societies. Due to the > 3% stroke and death rate reported by Gray et al., the societies do not support coverage for asymptomatic patients at high risk for surgery due to physiologic risk factors. They also note that this patient population should have a 5 year life expectancy to experience benefit from CAS and the 3 year outcomes data from SAPPHIRE bring into the question the 5 year survival rate. They assert that it is unclear if CAS or CEA is better that optimal medical therapy.

The societies have varying opinions on how to best define anatomic factors that make patients at high risk for CEA. The anatomic factors on which they agree are: 1) previous CEA with recurrent stenosis; 2) prior radiation therapy or radical surgery to the ipsilateral neck; 3) surgically inaccessible lesion above C2 (SNIS and SIR include lesions in the common carotid artery below the clavicle); 4) contralateral vocal cord palsy; and 5) presence of tracheostomy. The NVC includes contralateral occlusive lesions and SIR includes contralateral internal carotid artery occlusion. The SNIS includes prior carotid artery angioplasty and stenting with adjacent or in stent stenosis, and immobility of neck.

The societies all support coverage for CAS when performed without an embolic protection device (EPD) if the physician performing the procedure feels that EPD use is unsafe or technically impossible. All societies except SVIN specifically cite Barbato et al., 2008 and Perona et al., 2009, which show outcomes of CAS without EPDs to be similar to the best outcomes reported for CAS performed with EPDs. They contend that requiring facilities to be accredited and meet AHA benchmarks will incentivize physicians to appropriately use or not use EPDs.

The societies also support requiring independent neurological assessment pre and post procedure.

American Heart Association/American Stroke Association (AHA/ASA)

The AHA cites Massop et al., 2008, a review of SAPPHIRE WW and Gray et al., 2009, a review of CAPTURE 2 and EXACT. The AHA contends that these studies suggest that CAS is safe and effective when performed by the broader medical community and that CAS achieves AHA thresholds for 30-day stroke and death rates in a large patient cohort of the same age (under 80 years old). In addition, the AHA cites Chiam et al., 2008 and Velez et al., 2008 and states that the studies demonstrate 30-day stroke and death rates below the AHA thresholds in very elderly patients. However, the AHA stresses the importance of careful case selection in the very elderly in order to ensure that patients are not at high risk for CAS.

The AHA supports coverage of CAS for patients in whom revascularization is deemed appropriate by the primary physician and specialist treating them, when patients are at high risk for complications from CEA due to anatomic or comorbid clinical reasons. The AHA contends that anatomic and comorbid high surgical risk factors should be defined based on FDA labeling.

In the absence of head to head comparisons of CAS, CEA and medical therapy in octogenarians, the AHA supports coverage of CAS in octogenarians, especially those with anatomic high risk factors, as long as the patients are not at high risk for CAS.

The AHA recommends that CMS strongly encourage, or preferably, require participation in national CAS registries. Registries should require independent neurologic assessment for stroke and use uniform data elements and definitions. Outcomes should be evaluated pre, post and at 30 days post procedure with independent neurologic exams.

The AHA supports continued study of CAS versus CEA and medical therapy in high and normal risk patient populations, but asserts that expanded coverage should be established in a manner that "encourages completion of these trials."

American College of Cardiology (ACC), Society for Cardiovascular Angiography and Interventions (SCAI), Society for Vascular Medicine (SVM)

These professional societies jointly submitted comments to CMS requesting an expansion of coverage to all FDA approved indications: symptomatic patients at high risk for CEA with ≥ 50% stenosis and asymptomatic patients at high risk for CEA with ≥ 80% stenosis. They state that anatomic and comorbid conditions causing patients to be at high risk for CEA should be defined as in the 2007 consensus statement by Bates, et al.

They contend that coverage of all FDA approved indications is supported by clinical evidence. Yadav et al., 2004 shows CAS patients with any high risk factor to have similar outcomes to CEA in SAPPHIRE, which was accepted by the FDA for device approval. Gurm et al., 2008 through three year outcomes data from SAPPHIRE, confirms that CAS is durable and beneficial. Massop et al., 2008 shows from 30-day results of SAPPHIRE WW that stroke and death rates in all high risk patients was 4%. Gray et al., 2009 demonstrates that EXACT and CAPTURE 2 results meet or are below AHA thresholds (in patients under the age of 80). The societies also contend that various multispecialty society guidelines support coverage of all FDA approved indications.

The societies assert that good outcomes have been demonstrated in patients over 80 years old with 30-day stroke and death rates of 3.3%, 2.7% and 0.8% as shown in Chiam et al., 2008; Henry et al., 2008; and Velez et al., 2008 respectively. They state that published peer reviewed evidence does not support any age cut off for necessary revascularization but does show CAS to be preferred over CEA, with experienced operators and careful case selection.

The societies contend that all facilities and programs should undergo review and reaccreditation at regular intervals and should be required to show acceptable results in comparison with national benchmarks. They stress the need for robust data collection through formal CAS registries.

Society for Vascular Surgery (SVS)

The SVS supports an expansion of coverage for patients at high risk for CEA due to anatomic findings with carotid artery stenosis ≥ 80% as shown through angiography. Data from the SVS Vascular Registry (Sidawy et al., 2008) suggests that most providers are able to meet the 3% threshold. The SVS asserts that anatomic risk factors should be defined as: 1) prior radiation therapy to neck with permanent skin changes; 2) previous ablative neck surgery (e.g. radical neck dissection, laryngectomy); 3) common carotid stenosis below clavicle; 4) contralateral vocal cord paralysis; 5) presence of a tracheostomy stoma; and 6) extracranial ICA lesions convincingly above C2.

The SVS also contends that providers of CAS to asymptomatic patients must document 30-day stroke and death rates of < 3% in order to meet AHA thresholds for CEA. The SVS requests that CMS end the current data collection requirements and simultaneously require all facilities to report to formal society registries. The SVS also asserts that CMS require facilities to participate in a multispecialty accreditation program that would replace CMS facility approval and notes that such a program is under development.

Abbott

Abbott states that evidence supports an expansion of coverage to all high risk asymptomatic patients with ≥ 80% stenosis. They assert that these beneficiaries need access to CAS because CEA is contraindicated. They contend that recently published results from CAPTURE 2 and EXACT (Gray et al., 2009) and SAPPHIRE WW (Massop et al., 2008) demonstrate "the overall improvement of outcomes over time, as physicians continue to gain experience with the carotid stenting procedure." Abbott asserts that it is reasonable for CMS to base an expansion of coverage to high risk patients on these extensive real-world registry data.

Abbott contends that 30-day stroke and death rates reported by Gray et al. meet the AHA benchmarks of < 6% for symptomatic patients and < 3% for asymptomatic patients. For all high risk, symptomatic patients, the 30-day stroke/death rate was 6.4%; for non-octogenarian symptomatic patients it was 5.3%; and for symptomatic patients with anatomic risk factors it was 1.7%. For all high risk, asymptomatic patients the 30-day stroke/death rate was 3.2%; for non-octogenarian asymptomatic patients it was 2.9%; and for asymptomatic patients with anatomic risk factors it was 2.7%.

Abbott also recommends expanding the list of anatomic risk factors to include previous ablative neck surgery, tandem lesions and immobile neck as these three anatomic risk factors were included in many IDE trials.

Boston Scientific Corporation (BSC)

Boston Scientific Corporation supports coverage for all FDA approved indications. BSC contends that published evidence demonstrates that CAS achieves low levels of major adverse events in high risk patients; most specialty societies support coverage for all high risk patients; and CAS is preferred over CEA for very elderly patients at high risk for surgery. BSC also calls for an expansion of coverage because high risk patients have limited treatment options under the current policy.

BSC asserts that studies by Ouriel et al., 2001 and Wennberg et al., 1998, both of which examined CEA outcomes, demonstrate the difference in adverse outcomes between CEA and CAS, where higher rates of adverse outcomes were seen in CEA patients. In addition, BSC cites Gray et al., 2009 and Massop et al., 2008 stating that these studies show that CAS achieves AHA thresholds and that 30-day adverse event rates (excluding MI) are lower for high risk CAS patients than the high risk CEA patients (including MI) examined in the Ouriel et al. study.

BSC also references Chiam et al., 2008, Henry et al., 2008 and Velez et al.,2008, which show 30-day stroke and death rates in high surgical risk patients ≥ 80 years old to be 3.3%, 2.7% and 0.8% respectively to illustrate good outcomes in octogenarians. They state that the evidence does not support an age cut off for coverage of CAS and shows CAS is preferred over CEA.

Cordis Corporation

Cordis Corporation contends "that evidence strongly supports the improvement of health outcomes" in asymptomatic patients at high risk for surgery due to anatomic factors with ≥ 80% stenosis. Cordis cites 30-day results, in 2001 patients and 4007 patients respectively, from the SAPPHIRE trial reported by Massop et al. in 2009 and data presented at the 2009 ACC meeting and in an abstract (Metzger et al., 2009) published in JACC. Cordis asserts that all 30-day stroke and death rates for the FDA approved patient population come close to, meet, or are below the AHA thresholds. Cordis additionally cites data from EXACT and CAPTURE 2 (Gray et al., 2009) which also showed 30-day stroke and death rates close to, equal to, or below the AHA guidelines. When octogenarians are excluded from the data, the 30-day stroke and death rates are below the AHA guidelines at 5.3% for asymptomatic patients and 2.9% for symptomatic patients.

Cordis notes that while medical therapy should be a consideration for treatment of patients with asymptomatic carotid stenosis, there are two distinct problems with medical therapy. First, as discussed by Ansell, 2008, there is inconsistency in the definition of optimal medical therapy in treating patients with carotid stenosis. Second, as discussed by Touchette et al., 2008, patient compliance rates can be very low, as low as 42% in real world patients.

Cordis also references unpublished 3-year follow up data from SAPPHIRE that shows the rate of all stroke in anatomic high risk CAS patients to be 12% versus 13.2% for CEA.

Blue Cross and Blue Shield Association (BCBS)

The BCBS asserts that existing evidence does not support an expansion of coverage. They note that the AHA guidelines suggest that 5 years may be needed to realize the benefits of CAS in asymptomatic patients, and "among asymptomatic patients with carotid artery stenosis, a fine line divides potential benefit and harm." The BCBS also notes that the benefit of contemporary medical therapy compared with CAS in asymptomatic patients is not known. The BCBS contends that current evidence fails to provide adequate certainty that benefits outweigh harms in asymptomatic patients.

The BCBS expresses concern with the EXACT and CAPTURE 2 study results presented by Gray et al., 2009 which show, for asymptomatic patients with anatomic risk factors and > 80% stenosis, outcomes below the AHA threshold at 2.7%. The BCBS states that, "given the sample size of the subgroup, a simple simulation estimates a predictive probability of 69% that the periprocedural event rate is less that 3%. Accordingly, even assuming that achieving < 3% with a 5-year life expectancy might provide benefit, the level of decision certainty these data demonstrate does not appear adequate." The BCBS expresses further uncertainty because in the context of current optimal medical therapy, the 3% threshold may not be relevant.

The BCBS notes that the subgroup with anatomic high risk factors is not distinguishable in the 2009 report of SVS registry data by Sidawy et al. They contend that the outcomes are arguably generalizable and that Gray et al., 2009 found similar periprocedural event rates among asymptomatic patients with all risk factors. Therefore, outcomes do not support the contention that benefits of CAS outweigh possible harm in asymptomatic patients.

Comments without Evidence

Expand Coverage Policy

Twelve commenters contend that CMS should expand coverage of carotid artery stenting. Eleven commenters assert that coverage should be expanded to asymptomatic patients at high risk for surgery due to anatomic factors who have > 80% stenosis and four commenters request coverage for all FDA approved indications. Three commenters contend that coverage should be expanded to all asymptomatic patients with > 80% stenosis who are at high risk for surgery and one commenter asserts that coverage should be expanded to asymptomatic patients with > 80% stenosis. One commenter asserts that symptomatic stenosis > 50% should be covered and another commenter asserts that symptomatic and asymptomatic patients with > 50% stenosis and comorbidities should be covered. One commenter supports coverage of asymptomatic patients at high risk for surgery with > 80% stenosis after CEA. One commenter states that coverage should be expanded for patients at high risk for surgery with asymptomatic stenosis > 70% rather than > 80%. Another commenter contends that evidence supports coverage for anatomic and physiologic high risk patients as well as octogenarians and another commenter states that data shows CAS to be equal or superior to CEA when performed by properly trained and experienced interventionists.

One commenter states that symptomatic patients with anatomic risk factors or who are unsuitable for surgery with ipsilateral stenosis > 50% should be covered. Another commenter asserts that coverage should be expanded to asymptomatic patients under the age of 80 with > 80% stenosis as determined by CT angiogram or conventional angiogram. One commenter contends that anatomically difficult patients with no or low symptoms should be covered and another commenter contends that coverage should be expanded for difficult anatomic constraints. One commenter supports coverage of CAS for all patients and one commenter contends that coverage should be expanded for all high surgical risk patients. One commenter supports coverage for all asymptomatic high risk patients, one commenter supports coverage for all asymptomatic patients and another commenter asserts that coverage should be expanded for symptomatic and asymptomatic patients with anatomic high risk factors. One commenter asserts that coverage for PTA with embolic protection but without stenting should be covered in cases where a stent cannot be placed and for in-stent restenosis.

One commenter states that if CMS does not expand coverage for CAS then it should reconsider coverage for CEA.

Maintain Coverage Policy

Nine commenters state that CMS should not expand coverage and seven commenters warn that expanding coverage will lead to overuse or abuse of CAS. One commenter contends that data has not been convincing in support of CAS and one commenter cites the lack of data to support stenting in asymptomatic patients versus current medical therapy. Another commenter recommends that CMS not pay for completely asymptomatic patients. Four commenters request that no change in coverage be made until CREST and other similar trials are complete. Another commenter states that coverage should not be expanded until level 1 evidence from clinical trials demonstrate efficacy, preferably using QALYs.

Physician Involvement

Five commenters assert that a vascular surgeon should be required to make the determination that a patient is at high risk for surgery due to anatomic factors. One commenter states that a neurologist should be involved in pre-procedural approval and post-procedural care for CAS and CEA. One commenter recommends that CMS focus on the quality of an operator rather than limiting coverage for a "great" procedure. Another commenter asserts that physicians and patients should determine the best course of treatment and CMS should provide payment for what they deem best. One commenter contends that expanded coverage must be accompanied by a policing policy like requiring a surgical consultation for patients to undergo CAS.

Embolic Protection Use

One commenter questions the safety of distal embolic protection (DEP) devices stating that they are more dangerous than helpful and positive data favoring DEPs was manipulated by industry and self interested investigators. One commenter asserts that the use of embolic protection devices, whether distal or proximal, should continue to be required. One commenter requests that CMS revise the NCD to read "the use of an FDA-cleared EPD is required."

Benefits and Drawbacks of Coverage

One patient states that cost, mortality and stroke rates for CAS are twice that of surgery, while two commenters contend that CAS is low risk, less invasive and cost effective. One commenter notes that patients with anatomic high risk factors do not have good treatment options other than CAS and another commenter asserts that many high risk patients will not benefit from CAS because they may not live long enough to accrue the benefit by survivor analysis. One commenter contends that the delay in expanding payment (through CMS coverage) for CAS has saved many patients from unnecessary strokes.

Determination of Percent Stenosis

One commenter identifies the need for CMS to require an end diastolic velocity of > 140 cm/sec to determine actual percent stenoses in patients due to the current variability in the measurement and determination of percent stenosis. Another commenter contends that guidelines need to be established for how to calculate percent stenosis because currently there is too much variability and no regulations.

Comments with Evidence

Expand Coverage Policy

SAPPHIRE WW (Massop et al., 2009)
One commenter cites data from this study which demonstrated a composite stroke and death rate of 1.8% for asymptomatic patients with anatomic high risk factors and > 80% stenosis to support an expansion of coverage.

Gray et al, 2009
Two commenters cite the 30-day outcomes from the SAPPHIRE study which they contend show CAS to be equivalent or superior to CEA for asymptomatic and symptomatic high risk patients.

SPACE, EVA 3S
One commenter identifies flaws in these studies, stating that SPACE only used distal embolic protection in 1/3 of patients and EVA 3S had poor operator skills in the CAS arm which contributed to poor outcomes.

Maintain Coverage Policy

Sachinder et al., 2009 [SVS Vascular Meeting Presentation]
One commenter cites an abstract from the SVS vascular meeting that shows results of CEA in patients with anatomic high risk factors were similar to those performed on patients without high risk factors.

SPACE, EVA 3S
One commenter asserts that these two studies, which are far superior to post market studies, have demonstrated statistically significant stroke, death and restenosis rates in CAS patients versus CEA patients which does not support an expansion in coverage.

LoGerfo, 2007
One commenter cites this article which contends that SAPPHIRE data is tainted with conflict of interest, selection bias and statistical manipulation and therefore coverage should not be expanded based on SAPPHIRE study outcomes.

Sidawy et al., 2009
One commenter contends that data from this study does not support coverage of CAS for asymptomatic patient and that there is no agreement that recurrent stenosis places patients at higher risk for surgery.

VIII. CMS Analysis

National coverage determinations (NCDs) are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under title XVIII of the Social Security Act §1869(f)(1)(B). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions the expenses incurred for items or services must be "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." See §1862(a)(1)(A)of the Act. This section presents the agency's evaluation of the evidence considered and conclusions reached for the assessment.

The evidence base for carotid artery stenting continues to be of lower quality. There are a small number of randomized trials comparing CAS and CEA which have limited quality as we have discussed in prior decision memoranda. Acknowledging that existing case series and reviews may be markedly limited by selection bias, it is nonetheless informative in highlighting several other differences between treatments for carotid narrowing.

A. **Is the evidence sufficient to conclude that percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting for asymptomatic patients at high risk for CEAwith carotid artery stenosis ≥ 80% improves health outcomes compared to carotid endarterectomy or optimal medical therapy outside the IDE clinical trial or post approval study setting?**

Our initial decision to cover percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting for high risk asymptomatic patients with carotid artery stenosis ≥ 80% in clinical studies[8] (http://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=157) was based primarily on the SAPPHIRE trial (n =237 high risk patients with asymptomatic carotid artery stenosis ≥ 80%) results. At the time, we had many concerns about the quality of the SAPPHIRE trial and the lack of supporting evidence from other studies which led to the existing coverage restricted to IDE trials and post approval (post marketing) studies required by the FDA. We also noted the need for additional randomized controlled trials comparing CAS to both CEA and optimal medical therapy and the need for long term follow-up especially in asymptomatic patients who have a low risk of stroke. Since then no additional randomized controlled trials that have enrolled asymptomatic patients have been completed and published. SPACE and EVA-3S enrolled only symptomatic patients. The CAVATAS-MED trial reported by Ederle and colleagues started enrollment (1992) before the availability of carotid stents (1994) and did not provide any new data or evidence since the number of patients who underwent CAS and symptoms status were not reported. Although this study was recently published, we also do not believe it is directly applicable since the original CAVATAS (2001) was designed primarily to study angioplasty alone and not CAS (as noted in our prior decision). Several trials (CREST, ACT, TACIT, SPACE2) are ongoing or in development that will directly compare CAS, CEA and possibly optimal medical therapy.

One registry study by Sidawy and colleagues compared CAS to CEA and found a significantly higher rate of 30 day death, stroke or myocardial infarction in patients undergoing CAS compared to CEA (5.72% vs. 2.63%; P value < 0.001). Another CAS only registry study by de Donato and colleagues did not have a comparison group but reported 5 year outcomes for 3179 patients who underwent CAS. Of these, 1317 had symptomatic lesions ≥ 50% while 1862 had asymptomatic lesions ≥ 80%. For asymptomatic patients, death and stroke was 3.5% at year 1 increasing to 26.1% at year 5. The annual stroke rate was 1.9% which is higher than rates from prior CEA trials. This is concerning since the patients in this study were generally not high risk patients. The outcomes for asymptomatic patients were not significantly different (overlapping 95% confidence intervals) from the outcomes for symptomatic patients (2.5% and 3% at year 1 increasing to 16.7% and 18.7% at year 5, respectively), which is also concerning since symptomatic patients are known to be at higher risk for morbidity and mortality in general. One would expect based on prior evidence that asymptomatic patients would have better outcomes than symptomatic patients. Given that these two studies were registry studies, the evidence is less definitive but nonetheless concerning and further stress the need for additional long term data from randomized controlled trials.

Since our decision to cover CAS in clinical studies, several thousands of patients have undergone the procedure in registry studies with no comparison groups. Yet randomized controlled trials comparing CAS to CEA and CAS to optimal medical therapy, especially in asymptomatic patients, have not been completed and reported. We previously emphasized the need for well-designed and well-conducted randomized controlled trials with long term follow-up in past decisions, and this information is still needed. Naylor and colleagues also emphasized the ongoing need for randomized controlled trials: "At a time when evidence suggests that up to 94% of interventions may not benefit the patient, the authors urge that at least one of the randomised trials comparing CEA with CAS in asymptomatic patients includes an adequately powered third limb for BMT [best medical therapy]. Timely investment now could optimise patient care and resource utilisation for all of us in the future."

Since there are no new completed, published randomized trials and two nonsupportive registry studies, there is insufficient evidence to conclude that percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting for asymptomatic patients with carotid artery stenosis ≥ 80% improves health outcomes compared to carotid endarterectomy or optimal medical therapy outside the clinical trial or post approval study setting.

This conclusion is consistent with the Cochrane reviews by Ederle (2007, 2009) and the evidence based guidelines from the European Society for Vascular Surgery that noted: "Carotid artery stenting (CAS) should be performed only in high-risk for CEA patients, in high-volume centres with documented low peri-operative stroke and death rates or inside a randomized controlled trial." This is also consistent with the Blue Cross Blue Shield Association Technology Assessment Center (TEC) which has maintained that CAS with distal embolic protection does not meet TEC criteria since 2007 ("Available evidence does not support concluding that CAS with EPD improves the net health outcome among patients at average or increased medical risk." Full report at: http://www.bcbs.com/blueresources/tec/vols/22/22_01.pdf).

B. **Is the evidence sufficient to conclude that percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting for asymptomatic patients with anatomic high risk factors with carotid artery stenosis ≥ 80% and symptomatic patients with carotid artery stenosis 50-70% improves health outcomes?**

While we have not completely defined what constitutes high risk for CEA and have given discretion to classifications used in the published studies, we have been aware of the potential variability among patients considered to be at high risk. In the SAPPHIRE trial (Yadav, 2004), several criteria were used to classify high risk patient selection. These included: "Clinically significant cardiac disease (congestive heart failure, abnormal stress test, or need for open-heart surgery), Severe pulmonary disease, Contralateral carotid occlusion, Contralateral laryngeal-nerve palsy, Previous radical neck surgery or radiation therapy to the neck, Recurrent stenosis after endarterectomy, Age > 80 yr." The most common anatomic high risk factor was contralateral carotid occlusion (24%), followed by CEA restenosis (23%). Since then, there appears to be some coalescing of thought of researchers, professional societies and device manufacturers that the subset of anatomic high risk factors, such as contralateral carotid occlusion, prior radical neck surgery or radiation therapy to the neck, restenosis after CEA, high internal carotid lesions that are difficult to access surgically, presents more challenges to CEA than the subset with comorbid diseases, such as severe cardiac or pulmonary disease.

Although no randomized controlled trials have been reported that compare CAS to CEA or optimal medical therapy as noted above, several post approval studies and inhospital analyses have been published since our last reconsideration (October, 2008) that evaluated patients undergoing CAS and anatomic high risk factors. Three studies evaluated 30 day outcomes (Gray, 2009; Massop, 2009; Sidawy, 2009). The studies by de Donato (2009), Kawabata (2009), Simonetti (2009), Steppahcer (2009) and Vogel (2009) did not report outcomes for anatomic high risk factors.

Of the three registry studies that evaluated 30 day outcomes, the proportion of major adverse events (death, stroke and myocardial infarction) were 3.8% (95% CI, 3.4% to 4.3%); 4.4% (95% CI 3.5%, 5.3%); and 5.7% (confidence intervals not reported specifically), respectively. Long term results were not reported.

In the EXACT/CAPTURE 2 study, Gray and colleagues reported: "The 30-day rate of death and stroke for the 60 symptomatic patients with anatomic factors was 1.7% (95% CI, 0.0% to 8.9%); the single stroke was adjudicated as major. The 30-day rate of death and stroke for the 371 asymptomatic patients with anatomic high -risk features was 2.7% (95% CI, 1.3% to 4.9%), of which 78% were minor." In the SAPPHIRE WW study, Massop and colleagues reported: "Asymptomatic patients with anatomic risk factors had a 30-day stroke and death rate of 1.8% while symptomatic patients with anatomic risk factors had a 30-day rate of 4.5% (P = 0.0589)." The death or stroke rate for patients with pure anatomic risk factors was 2.5% (18/716). The studies by Sidawy (2009), Steppacher (2009) and Vogel (2009) did not report specific results for anatomic high risk factors.

Of the two studies that reported results for patients with anatomic high risk factors, combined 30 day death and stroke was 2.6% in the Gray study and 2.5% in the Massop study. The proportion of patients classified as anatomic high risk was about 7% (431/6320) in the Gray study and 37% (716/1961) in the Massop study. This large discrepancy needs further consideration. In the SAPPHIRE trial (2004), the combined proportion of patients with the two most common high risk criteria, contralateral carotid occlusion or recurrent stenosis after endarterectomy, was up to 46% (if the separate rates of 24% and 22% did not overlap). The proportion of patients with anatomic high risk criteria in the SAPPHIRE WW registry was consistent with the SAPPHIRE trial; however, the markedly lower proportion (7%) in the EXACT/CAPTURE 2 registry suggests either classification / reporting errors or selection bias (selective enrollment of lower risk patients).

The study by Gray and colleagues reported that CAS outcomes have met the AHA/ASA recommendations for high surgical risk patients < 80 years of age. Since outcomes for patients ≥ 80 years old were worse, the selective exclusion of this subgroup of patients also raises questions. Exclusion of 23-24% of the patients presents great potential for selection bias or extreme confounding in the results. CAS continues to be performed in large numbers for patients ≥ 80 years, so results excluding these patients do not accurately reflect current practice realities. The study by Gray presents interesting findings from registry data that generate hypotheses but further evidence from clinical trials is needed to confirm these findings. The study by Massop did not report results by symptoms or by age other than noting age ≥ 80 years was a significant predictor of 30 day major adverse events.

For symptomatic and asymptomatic patients with anatomic high risk factors, the 30 day adverse event rates appear to approach the AHA/ASA recommendations; however, the inherent flaws of registry studies, such as lack of control groups, patient selection bias and voluntary data submission, limit the interpretation of the published death and stroke rates and reduce the strength of this evidence considerably. Results of subgroup analyses of registry studies are even more problematic to interpret and are at best only suggestive.

In summary, while available evidence suggests the potential for PTA of the carotid artery concurrent with stenting for asymptomatic patients with anatomic high risk factors with carotid artery stenosis ≥ 80% and symptomatic patients with carotid artery stenosis 50-70% to improve health outcomes, currently published data are not sufficient to expand coverage beyond the currently covered patient populations. The current evidence, which has been collected under the authority of coverage for post-approval studies, is insufficient to conclude that PTA of the carotid artery concurrent with stenting for asymptomatic patients with anatomic high risk factors with carotid artery stenosis ≥ 80% and symptomatic patients with carotid artery stenosis 50-70% can be performed with procedural complication rates to meet AHA/ASA guidelines. Due to the lower quality and limited quantity of published, peer-reviewed evidence available addressing the patient populations under consideration, CMS has determined that an expansion of coverage is not reasonable and necessary and has decided to make no changes to the NCD.

Carotid Interventions in Patients ≥ 80 years of Age

Most of the large trials that demonstrated the benefits of CEA excluded patients ≥ 80 years of age. The SAPPHIRE trial (Yadav, 2004) showed that patients ≥ 80 years of age had significantly higher 30 day adverse events.A number of registry studies (SAPPHIRE WW, EXACT/CAPTURE 2, SVS Vascular Registry) and one meta-analysis (Usman, 2009) have also shown that patients ≥ 80 years of age have higher rates of 30 day adverse events. The 2006 AHA/ASA guidelines noted: "Despite the need to consider different interventional approaches, some trials do not include a sufficient number of subjects > 80 years of age to fully evaluate the efficacy of a therapy within this important subgroup." While cautions have often been raised, the numbers of patients ≥ 80 years undergoing CAS have increased. In SAPPHIRE trial, the proportion of CAS patients > 80 years was 19% (32/166). This proportion increased to 26% (520/2001) in SAPPHIRE WW, 24% (511/2145) in EXACT, 24% (829/3,500) in CAPTURE and 22% (938/4175) in CAPTURE 2. As with many procedures in the elderly, the key question is should it be done and not whether it can be done. To answer this for patients ≥ 80 years of age, a consideration of long term health outcomes and life expectancy is needed in addition to the peri-procedural health outcomes reported in various case series and registry studies.

Since the natural history of disease on optimal medical therapy is unknown for these patients, long term outcomes are extremely important to determine whether CAS should be performed. No published study has presented long term outcomes for patients ≥ 80 years. For carotid interventions, a life expectancy of at least 5 years is recommended by the AHA/ASA. However, if the life expectancy is less than 5 years, the potential benefits of carotid interventions may not be realized (to overcome the peri-procedural adverse events). For asymptomatic patients, CAS enters the realm of primary prevention of stroke and a more rigorous evaluation of health risks and benefits with definite evidence is desperately needed.

Until long term results from randomized controlled trials comparing CAS to optimal medical therapy are available for this important subgroup, CAS and possibly any carotid intervention should rarely, if at all, be performed in patients ≥ 80 years of age especially for asymptomatic individuals.

Embolic Protection Devices

As carotid stenting continues to be widely performed, new embolic protection devices, without specific accompanying stent systems, have been developed and several have received FDA 510(k) clearance as substantially equivalent to previous embolic protection devices. In order to avoid confusion and clearly include these newer devices, we are proposing to revise the NCD language addressing EPDs to specifically include coverage of "FDA approved or cleared embolic protection devices." As EPDs that are designed to be placed proximally are being developed and cleared by the FDA, we propose to remove "distal" from references to embolic protection devices to avoid confusion.

IX. Conclusion

As we have concluded in the last two decision memoranda, "for CAS to be considered an alternative to CEA and improve health outcomes for asymptomatic patients with asymptomatic stenosis > 80%, the perioperative morbidity and mortality rates should be less than 3%." For symptomatic patients with stenosis > 50%, the benchmark is less than 6% death and stroke within 30 days of the procedure. The body of randomized trials and post approval studies does not demonstrate that CAS can be performed at that level. Although performance continues to improve, the greatest concern is for asymptomatic patients who are at low risk and may benefit from medical therapy. Some experts have questioned the 3% value, as the benefits of medical therapy may have improved. This continues to highlight the need for a randomized trial comparing CAS with optimal medical therapy. Since current evidence is inadequate, CMS proposes not to expand coverage of PTA concurrent with carotid artery stenting.

X. Proposed Decision

The Centers for Medicare and Medicaid Services (CMS) proposes the following:

Based on the Food and Drug Administration (FDA) clearance of new embolic protection devices, we propose to revise the NCD language regarding embolic protection devices as follows:

Coverage is limited to procedures performed using FDA approved carotid artery stents and FDA approved or cleared embolic protection devices.

The use of an FDA approved or cleared embolic protection device is required. If deployment of the embolic protection device is not technically possible, then the procedure should be aborted given the risks of CAS without embolic protection.

We propose to make no changes in coverage of patient groups for percutaneous transluminal angioplasty (PTA) of the carotid artery concurrent with stenting (Medicare National Coverage Determination (NCD) Manual 20.7B4). We propose to retain our existing coverage for the following with a slight revision to the language regarding embolic protection devices:

- Patients who are at high risk for carotid endarterectomy (CEA) and who also have symptomatic carotid artery stenosis ≥70%. Coverage is limited to procedures performed using FDA-approved carotid artery stenting systems and FDA-approved or cleared embolic protection devices;
- Patients who are at high risk for CEA and have symptomatic carotid artery stenosis between 50% and 70%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on carotid artery stenting (CAS) post-approval studies (Medicare NCD Manual 20.7B);
- Patients who are at high risk for CEA and have asymptomatic carotid artery stenosis ≥80%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on CAS post- approval studies (Medicare NCD Manual 20.7B).

We are requesting public comments on this proposed determination pursuant to Section 1862(l) of the Social Security Act. After considering the public comments, we will make a final determination and issue a final decision memorandum.

Appendix A: General Methodological Principles of Study Design

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine whether: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

CMS normally divides the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the relevance of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's risks and benefits.

The issues presented here represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has unique methodological aspects.

1. Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to help ensure adequate numbers of patients are enrolled to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias)
- Co-interventions or provision of care apart from the intervention under evaluation (confounding)
- Differential assessment of outcome (detection bias)
- Occurrence and reporting of patients who do not complete the study (attrition bias)

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

- Randomized controlled trials
- Non-randomized controlled trials
- Prospective cohort studies

- Retrospective case control studies
- Cross-sectional studies
- Surveillance studies (e.g., using registries or surveys)
- Consecutive case series
- Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study's selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess the evidence.

2. Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens, and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease, and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing, and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow -up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage decisions for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation), and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations because one of the goals of our determination process is to assess health outcomes. We are interested in the results of changed patient management not just altered management. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

3. Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Improved health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. For most determinations, CMS evaluates whether reported benefits translate into improved health outcomes. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

Appendix B: Proposed Changes to the National Coverage Determination

Effective XX, 2009, Medicare covers PTA of the carotid artery concurrent with the placement of an FDA-approved carotid stent with embolic protection for the following:

- Patients who are at high risk for carotid endarterectomy (CEA) and who also have symptomatic carotid artery stenosis ≥70%. Coverage is limited to procedures performed using FDA-approved carotid artery stenting systems and *FDA-approved or cleared* embolic protection devices;
- Patients who are at high risk for CEA and have symptomatic carotid artery stenosis between 50% and 70%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on carotid artery stenting (CAS) post-approval studies (Medicare NCD Manual 20.7B);
- Patients who are at high risk for CEA and have asymptomatic carotid artery stenosis ≥80%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the NCD on CAS post- approval studies (Medicare NCD Manual 20.7B).

Coverage is limited to procedures performed using FDA approved carotid artery stents and *FDA approved or cleared* embolic protection devices.

The use of a*n FDA approved or cleared* embolic protection device is required. If deployment of the embolic protection device is not technically possible, then the procedure should be aborted given the risks of CAS without embolic protection.

Patients at high risk for CEA are defined as having significant comorbidities and/or anatomic risk factors (i.e., recurrent stenosis and/or previous radical neck dissection), and would be poor candidates for CEA.

Significant comorbid conditions include but are not limited to:

- congestive heart failure (CHF) class III/IV;
- left ventricular ejection fraction (LVEF)< 30%;
- unstable angina;
- contralateral carotid occlusion;
- recent myocardial infarction (MI);
- previous CEA with recurrent stenosis;
- prior radiation treatment to the neck; and
- other conditions that were used to determine patients at high risk for CEA in the prior carotid artery
- stenting trials and studies, such as ARCHER, CABERNET, SAPPHIRE, BEACH, and
- MAVERIC II.

Symptoms of carotid artery stenosis include carotid transient ischemic attack (distinct focal neurological dysfunction persisting less than 24 hours), focal cerebral ischemia producing a nondisabling stroke (modified Rankin scale < 3 with symptoms for 24 hours or more), and transient monocular blindness (amaurosis fugax). Patients who have had a disabling stroke (modified Rankin scale ≥ 3) shall be excluded from coverage.

The determination that a patient is at high risk for CEA and the patient's symptoms of carotid artery stenosis shall be available in the patient medical records prior to performing any procedure.

The degree of carotid artery stenosis shall be measured by duplex Doppler ultrasound or carotid artery angiography and recorded in the patient's medical records. If the stenosis is measured by ultrasound prior to the procedure, then the degree of stenosis must be confirmed by angiography at the start of the procedure. If the stenosis is determined to be less than 70% by angiography, then CAS should not proceed.

In addition, CMS has determined that CAS with embolic protection is reasonable and necessary only if performed in facilities that have been determined to be competent in performing the evaluation, procedure and follow-up necessary to ensure optimal patient outcomes. Standards to determine competency include specific physician training standards, facility support requirements and data collection to evaluate outcomes during a required reevaluation.

CMS has created a list of minimum standards modeled in part on professional society statements on competency. All facilities must at least meet CMS's standards in order to receive coverage for carotid artery stenting for high risk patients.

- Facilities must have necessary imaging equipment, device inventory, staffing, and infrastructure to support a dedicated carotid stent program. Specifically, high-quality X-ray imaging equipment is a critical component of any carotid interventional suite, such as high resolution digital imaging systems with the capability of subtraction, magnification, road mapping, and orthogonal angulation.

- Advanced physiologic monitoring must be available in the interventional suite. This includes real time and archived physiologic, hemodynamic, and cardiac rhythm monitoring equipment, as well as support staff who are capable of interpreting the findings and responding appropriately.

- Emergency management equipment and systems must be readily available in the interventional suite such as resuscitation equipment, a defibrillator, vasoactive and antiarrhythmic drugs, endotracheal intubation capability, and anesthesia support.

- Each institution shall have a clearly delineated program for granting carotid stent privileges and for monitoring the quality of the individual interventionalists and the program as a whole. The oversight committee for this program shall be empowered to identify the minimum case volume for an operator to maintain privileges, as well as the (risk-adjusted) threshold for complications that the institution will allow before suspending privileges or instituting measures for remediation. Committees are encouraged to apply published standards from national specialty societies recognized by the American Board of Medical Specialties to determine appropriate physician qualifications. Examples of standards and clinical competence guidelines include those published in the December 2004 edition of the American Journal of Neuroradiology, and those published in the August 18, 2004 Journal of the American College of Cardiology.

- To continue to receive Medicare payment for CAS under this decision, the facility or a contractor to the facility must collect data on all carotid artery stenting procedures done at that particular facility. This data must be analyzed routinely to ensure patient safety. This data must be made available to CMS upon request. The interval for data analysis will be determined by the facility but shall not be less frequent than every 6 months.

Since there currently is no recognized entity that evaluates CAS facilities, CMS has established a mechanism for evaluating facilities. Facilities must provide written documentation to CMS that the facility meets one of the following:

1. The facility was an FDA approved site that enrolled patients in prior CAS IDE trials, such as SAPPHIRE, and ARCHER;

2. The facility is an FDA approved site that is participating and enrolling patients in ongoing CAS IDE trials, such as CREST;

3. The facility is an FDA approved site for one or more FDA post approval studies; or

4. The facility has provided a written affidavit to CMS attesting that the facility has met the minimum facility standards. This should be sent to:

   Director, Coverage and Analysis Group
   7500 Security Boulevard, Mailstop C1-09-06
   Baltimore, MD 21244.

The letter must include the following information:
Facility's name and complete address;
Facility's Medicare provider number;
Point-of-contact for questions with telephone number;
Discussion of how each standard has been met by the hospital;
Mechanism of data collection of CAS procedures; **and**
Signature of a senior facility administrative official.

A list of certified facilities will be made available and viewable at: http://www.cms.hhs.gov/MedicareApprovedFacilitie/CASF/list.asp#TopOfPage. In addition, CMS will publish a list of approved facilities in the Federal Register.

Facilities must recertify every two (2) years in order to maintain Medicare coverage of CAS procedures. Recertification will occur when the facility documents that and describes how it continues to meet the CMS standards.

The process for recertification is as follows:

At 23 months after initial certification:

- Submission of a letter to CMS stating how the facility continues to meet the minimum facility standards as listed above.

At 27 months after initial certification:

- Submission of required data elements for all CAS procedures performed on patients during the previous two (2) years of certification.
- Data elements: Patients' Medicare identification number if a Medicare beneficiary;
  Patients' date of birth;
  Date of procedure;
  Does the patient meet high surgical risk criteria (defined below)?
    - Age ≥80;
    - Recent (< 30 days) Myocardial Infarction (MI);
    - Left Ventricle Ejection Fraction (LVEF) < 30%;
    - Contralateral carotid occlusion;
    - New York Heart Association (NYHA) Class III or IV congestive heart failure;
    - Unstable angina: Canadian Cardiovascular Society (CCS) Class III/IV;
    - Renal failure: end stage renal disease on dialysis;
    - Common Carotid Artery (CCA) lesion(s) below clavicle;
    - Severe chronic lung disease;
    - Previous neck radiation;
    - High cervical Internal Carotid Artery (ICA) lesion(s);
    - Restenosis of prior carotid endarterectomy (CEA);
    - Tracheostomy;
    - Contralateral laryngeal nerve palsy.

  Is the patient symptomatic (defined below)?
    - Carotid Transient Ischemic Attack (TIA): distinct focal neurologic dysfunction persisting less than 24 hours;
    - Non-disabling stroke: Modified Rankin Scale < 3 with symptoms for 24 hours or more;
    - Transient monocular blindness: amaurosis fugax.

  Modified Rankin Scale score if the patient experienced a stroke;
  % stenosis of stented lesion(s) by angiography;
  Was embolic protection used?
  Were there any complications during hospitalization (defined below)?
    - All stroke: an ischemic neurologic deficit that persisted more than 24 hours;
    - MI;
    - All death.

Recertification is effective for two (2) additional years during which facilities will be required to submit the requested data every April 1 and October 1.

CMS will consider the approval of national carotid artery stenting registries that provide CMS with a comprehensive overview of the registry and its capabilities, and the manner in which the registry meets CMS data collection and evaluation requirements. Specific standards for CMS approval are listed below. Facilities enrolled in a CMS approved national carotid artery stenting registry will automatically meet the data collection standards required for initial and continued facility certification. Hospitals' contracts with an approved registry may include authority for the registry to submit required data to CMS for the hospital. A list of approved registries will be available on the CMS coverage website.

As noted above, CMS will approve national registries developed by professional societies and other organizations and allow these entities to collect and submit data to CMS on behalf of participating facilities to meet facility certification and recertification requirements. To be eligible to perform these functions and become a CMS approved registry, the national registry, at a minimum, must be able to:

1. Enroll facilities in every US state and territory;

2. Assure data confidentiality and compliance with HIPAA;

3. Collect the required CMS data elements as listed in the above section;

4. Assure data quality and data completeness;

5. Address deficiencies in the facility data collection, quality and submission;

6. Validate the data submitted by facilities as needed;

7. Track long term outcomes such as stroke and death;

8. Conduct data analyses and produce facility specific data reports and summaries;

9. Submit data to CMS on behalf of the individual facilities;

10. Provide quarterly reports to CMS on facilities that do not meet or no longer meet the CMS facility certification and recertification requirements pertaining to data collection and analysis.

Registries wishing to receive this designation from CMS must submit evidence that they meet or exceed our standards. Though the registry requirements pertain to CAS, CMS strongly encourages all national registries to establish a similar mechanism to collect comparable data on CEA. Having both CAS and CEA data will help answer questions about carotid revascularization, in general, in the Medicare population.

CAS for patients who are not at high risk for CEA remains covered only in FDA-approved Category B IDE clinical trials under 42 CFR 405.201.

CMS has determined that PTA of the carotid artery concurrent with the placement of an FDA-approved carotid stent is not reasonable and necessary for all other patients.

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[3] XACT post approval study information at: http://www.clinicaltrials.gov/ct2/show/NCT00287508

[4] ACCULINK post approval study information at: http://www.clinicaltrials.gov/ct2/show/NCT00180492

[5] The SAPPHIRE trial was "was a multicenter, prospective trial conducted at 29 centers between 2000 and 2002 to compare outcomes of CAS versus CEA in high-surgical risk patients . Entry criteria included either ≥50% carotid stenosis if symptomatic or ≥80% carotid stenosis if asymptomatic." (Yadav, 2004; Gurm, 2008) SAPPHIRE information at: http://www.clinicaltrials.gov/ct2/show/NCT00231270?term=sapphire&rank=12

[6] SAPPHIRE WW information at: http://www.clinicaltrials.gov/ct2/show/NCT00403078?term=sapphire&rank=4

[7] Grade Recommendation
A - Based on the criterion of at least one randomized, controlled clinical trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.
B - Based on well-conducted clinical studies but no good-quality randomized clinical trials on the topic of recommendation.
C - Based on evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. (i.e., no applicable studies of good quality)

[8] Patients who are at high risk for CEA and have asymptomatic carotid artery stenosis ≥80%, in accordance with the Category B IDE clinical trials regulation (42 CFR 405.201), as a routine cost under the clinical trials policy (Medicare NCD Manual 310.1), or in accordance with the National Coverage Determination on CAS post approval studies (Medicare NCD Manual 20.7).

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